

**AMENDMENTS TO THE DRAWINGS**

The attached sheet of drawings includes changes to Figures 5 and 6. This sheet, which includes Figures 5 and 6, replaces the original sheet including Figures 5 and 6.

Attachment: Replacement Sheet

**REMARKS**

Favorable reconsideration of this application, in light of the preceding amendments and following remarks, is respectfully requested.

Claims 1-28 are pending in this application, of which claims 11-20 are withdrawn as being directed to a non-elected invention. By this Amendment, claims 1 and 26 are amended; and FIGS. 5 and 6 are amended to replace "t[s]" with "t[ms]". No new matter is added. Claims 1 and 26 are the independent claims.

Applicants note with appreciation the Examiner's acknowledgement that certified copies of all priority documents have been received by the U.S.P.T.O.

Applicants also respectfully note the present action indicates that the drawings have been accepted by the Examiner.

**Claim Rejections - 35 U.S.C. § 112**

***I. First Paragraph***

Claims 1-10, 21-25, and 28 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Applicants respectfully traverse this rejection for the reasons discussed below.

In rejecting claim 1 for lack of enablement, in the Response to Argument section, pages 3 and 4, in the Final Office Action mailed February 16, 2011, the Examiner asserted,

...Figure 3 contains multiple pulse trains (i.e., 31-34). Additionally, figure 3 actually has a set measuring phase that amounts to 0.25 sec and a set relaxation phase 0.75 sec. The current measurement takes place 0.24 sec after the start of the measuring phase (see applicant's PG Pub section 0054). Therefore, with regard to figure 3, there is no clear direction as

to which pulse train, numerals 31-34 is preferred or as to how one skilled in the art would select an appropriate pulse length to arrive at a desired pulse train....

Applicants respectfully submit that claim 1 is fully enabled by the instant application as originally filed.

As shown in FIG. 3, the current density is a function of the pAP concentration in the solution for various *pulse trains* depicted by characteristic lines **31 to 34**. The measuring phase amounts to 0.25 s and the relaxation phase amounts to 0.75 s (*that provides a measurement of 1 s*). The measurement of current takes place 0.24 s after the start of the measuring phase. The oxidation potential during the measuring phase relative to the redox potential amounts to +200 mV. The potential has been varied during the relaxation phase. It assumes values between -300 mV and 0 mV relative to the redox potential.

For example,  $\Phi_{\text{red}}/\Phi_{\text{ox}}$  may be:

-300 mV/200 mV for characteristic line **31**;

-200 mV/200 mV for characteristic line **32**;

-100 mV/200 mV for characteristic line **33**; and

0 mV/200 mV for characteristic line **34**.

As such, given these parameters, different rises in the current density in terms of its functional dependence depends upon the concentration pAP result. Further, the rise in the current density with the pAP-concentration, that is, the sensitivity of the measurement, increases constantly with a potential that is becoming negative during the relaxation phase. Moreover, plotting the rise against the relaxation potential in accordance with **FIG. 4** clearly shows, by way of characteristic line 41, the advantageous effect of pulsed redox-cycling.

Further, as described in paragraph [0063] in the specification, experiments with constant concentration may provide information about the signal constancy over time. For instance, when the concentration amounted to 50 pM pAP, the potential during the measuring phase amounted to +200 mV. Also, the duration of the measuring phase amounted to 250 ms, in which case the measurement of current took place after 240 ms. The potential during the relaxation phase amounted in the first experiment to 0V versus  $\Phi_0$  in the second experiment to -300 mV versus  $\Phi_0$ . The duration of the relaxation phase was varied between 250 ms and 4.75 s.

Accordingly, based on the above information, FIG. 9 illustrates a diagram  $U_{out} \sim I$  versus (t) demonstrating that the first (positive) half cycle is 0.25s long and the second (negative) half cycle is 0.75s. As shown in FIG. 9, there are 3 cycles in sum equalling 3 s - one cycle (positive + negative part) being 1 s. Further, as mentioned in paragraph [0063], the measurement takes place after 240 ms. As a result, the measurement takes place from 240 ms to 250 ms (i.e., the flat part of the positive part of a cycle in FIG. 9), and lasts 10 ms.

Accordingly, in view of the above, one skilled in the art may measure pulse trains with 1 s cycle and 10 ms measurement at the end of the positive part of the cycle, resulting in FIG. 3.

Therefore, Applicants respectfully submits that the originally filed disclosure does provide one skilled in the art the ability to arrive at a specific pulse length or provide one skilled in the art with a method by which a pulse length to be selected. Accordingly, the scope of *at least* claim 1 is entirely commensurate with, and is fully enabled by, the original disclosure.

In addition, in regard to FIGS. 5 and 6, the Examiner asserted,

...with regard to figures 5 and 6, numerals 51-54 and 61-64 are the results of different relaxation phase durations. There is no indication of which one is preferred or as to how one skilled in the art would select an appropriate relaxation phase duration ....<sup>1</sup>

Applicants submit that Figures 5 and 6 adequately describe the appropriate relaxation phase duration, and respectfully submit that it is well within the ability of one of ordinary skill in the art to perform the method, without undue experimentation. That is, with regard to FIG. 5, it is a graphic representation of the dependence of the current density ( $j$ ) upon time ( $t$ ). Characteristic lines **51 to 54** result for different relaxation-phase durations  $\Delta t_{\text{red}}$ , that is, in particular between 0.255 and 4.755. The currents fall greatly within the first 10 s of measurement. Given a length of the relaxation phase of 0.25 s, the decrease amounts to 14 pA/cm<sup>2</sup> in 10 s. If the duration of the relaxation phase is increased to 4.75 s, the decrease in the signal reduces to 9 pA/cm<sup>2</sup> in 10 s. The shorter the duration of the relaxation phase, the greater this decrease in the signal is with time.

Further, if the potential is now reduced during the relaxation phase to -300 mV, the signal constancy is significantly improved. This follows in particular from FIG. 6 which shows a representation that corresponds to FIG. 5 with characteristic lines **61 to 64** for the same parameters of the relaxation phases  $\Delta t_{\text{red}}$ .

Furthermore, the Examiner asserted that:

...While according to applicant's specification 1 Hz and a relaxation potential of -300 mV create a signal drop and a drop in error of approximately 1% of the expected measured value,

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<sup>1</sup> See Final Office Action mailed February 16, 2011, pages 3 and 4.

this would be helpful if one were to select the frequency and potential, not the pulse length ....<sup>2</sup>

Applicants submit that frequency and potential do correspond to "pulse length." For instance, as discussed above regarding the pulse length for FIGS. 5 and 6, it describes measuring the frequency as "s". That is, one skilled in the art would appreciate that  $1 \text{ Hz} = 1/\text{s}$ . In other words, a frequency of 1 Hz is the value of 1 s with frequency = 1/time. Moreover, paragraph [0017] describes the time resolution of measurement amounting to 1 to 2 Hz; paragraph [0021] describes the measured frequency of  $\geq 1 \text{ Hz}$ ; and paragraph [0066] describes the measured frequency of 1 Hz; and claim 5 recites the repetition rate for the pulsed redox-cycling amounts to at least 1/10 Hz.

Accordingly, in view of above, and in connection with paragraphs [0054] and [0063], one skilled in the art would be able to determine the measurement.

Therefore, since it is well within the ability of one of ordinary skill in the art to perform the method recited in claim 1 without undue experimentation, Applicants respectfully submit that there is no reasonable basis for maintaining this rejection. Therefore, Applicants respectfully request that this rejection of claim 1, and of claims 2-10, 21-25, and 28 depending therefrom, be reconsidered and withdrawn.

## ***II. Second Paragraph***

Claims 1, 2-10, 21-25, and 28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection for the reasons discussed below.

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<sup>2</sup> See Final Office Action mailed February 16, 2011, pages 5 and 6.

Applicants have amended the claims, taking into consideration the Examiner's comments, to obviate the rejections. In particular, claim 1 has been amended to include "the measurements of the oxidation currents and the reduction currents."

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, are respectfully requested.

**Claim Rejections - 35 U.S.C. § 102**

Claims 1-4 and 28 are rejected under 35 U.S.C. § 102(b) as being anticipated by J. Electroanal. Chem. 287, 1990, 349-362 to Gunasingham et al. (hereinafter "Gunasingham"). Applicants respectfully traverse this rejection for the reasons discussed below.

Applicants respectfully submit that the Gunasingham reference fails to disclose or suggest, *inter alia*:

selecting relaxation-phase pulse lengths so that, at the end of the pulse, a concentration gradient is relaxed such that at a beginning of a following measuring phase, the change in concentration of the mediator, brought about by the measurement of the mediator, is reversible,

as recited in amended claim 1.

In other words, claim 1 recites that (in connection with measuring-phase and relaxation-phase) there has to be an oxidation potential pulse followed by a pulse at a reducing potential or ***vice versa*** in the measuring-phase and relaxation-phase,

In the outstanding Final Office Action, the Examiner contends that the "TTF must be measured since the entire system of Gunasingham is subjected to pulsed detection (ie., a measuring and relaxation phase, see figure 1)."<sup>3</sup> Although

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<sup>3</sup> See Final Office Action mailed February 16, 2011, page 6, paragraph 10.

Gunasingham may disclose a “pulsed” detection, it is submitted that Gunasingham is silent in teaching or suggesting “at a beginning of a following measuring phase, the change in concentration of the mediator, brought about by the measurement of the mediator, **is reversible**,” as taught by claim 1.

Further, because the substance in Gunasingham to be measured is “glucose,” there is nothing regarding the relation of the base potential (of Fig. 1) to the oxidation or reduction potential of measured substance glucose. Gunasingham merely discloses the different oxidation and reduction potentials of TTF (base potential in Fig. 1 is reduction potential of TTF) and glucose (pulse potential in Fig. 1 is oxidation potential of glucose at enzyme glucose oxidase electrode). This is not the same as disclosing an oxidation potential pulse followed by a pulse at a reducing potential or vice versa.

Moreover, Applicants respectfully submit that Gunasingham also fails to teach or suggest “selecting measuring-phase pulse lengths so that, at the end of the pulse, a capacitive current is small in **comparison with a Faraday current**,” as recited in claim 1. Specifically, Applicants submit that Gunasingham is completely silent of teaching or suggesting of comparing the capacitive current to a Faraday current.

Therefore, contrary to the Examiner’s contention, the Gunasingham reference does not disclose or suggest each and every element of claim 1.

Since the Gunasingham reference fails to disclose each and every element of claim 1, it cannot provide a basis for a rejection under 35 U.S.C. § 102(b) and, thus, is allowable. Claims 2-4 and 28 depend from amended claim 1 and, therefore, allowable for similar reasons to those discussed above with respect to claim 1.

For at least these reasons, the Examiner is respectfully requested to reconsider and withdraw the § 102(b) rejection of claims 1-4 and 28.



Claims 26 and 27 are rejected under 35 U.S.C. § 102(b) as being anticipated by Anal. Chem. 1989, 61 2566-2570 to Bindra et al. ("the Bindra reference"); and Claims 26 and 27 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,391,558 to Henkens et al. ("the Henkens reference"). Applicants respectfully traverse these rejections for the reasons discussed below.

For the similar reasons as discussed above regarding claim 1, Applicants respectfully submit that claim 26 is similarly allowable. In particular, claim 26 recites, *inter alia*:

a device for selecting, in this connection, the measuring-phase pulse lengths so that, at the end of the pulse, a capacitive current is small in comparison with a Faraday current;

a device for selecting the relaxation-phase pulse lengths so that, at the end of the pulse, the concentration gradient is relaxed so that at the beginning of a following measuring phase, the change in concentration of the mediator, brought about by the consumption of the mediator by the measurement itself, is reversible.

Applicants respectfully submit that the Bindra and the Henkens references similarly fail to provide the teachings, discussed above, that are missing from the Gunasingham reference.

In view of the above, Applicants respectfully submit that the Bindra and the Henkens references fail to teach or suggest *all* of the elements of claim 26. Thus, no *prima facie* case of anticipation has been established. Accordingly, claim 26 is allowable over the Bindra and the Henkens references. Dependent claim 27 depends from claim 26 and is allowable for at least the reasons that claim 26 is allowable. Therefore, Applicants respectfully request that the rejection of claims 26 and 27 under 35 U.S.C. § 103(a) be favorable reconsidered and withdrawn.

**Claim Rejections - 35 U.S.C. § 103**

Claims 5, 10, and 21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gunasingham et al. in view of Bindra et al. Applicants respectfully traverse this rejection for the reasons discussed below.

Claims 5, 10, and 21 are believed to be allowable for at least the reasons set forth above regarding claim 1. The Bindra reference fails to provide the teachings noted above as missing from the Gunasingham reference. Since claims 5, 10, and 21 are patentable at least by virtue of their dependency on claim 1, Applicants respectfully request that the rejection of claims 5, 10, and 21 under 35 U.S.C. § 103(a) be withdrawn.

Claims 6-8 and 22-24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gunasingham et al. in view of WO 01/21827 to Buck et al. ("the Buck reference"). Applicants respectfully traverse this rejection for the reasons discussed below.

Claims 6-8 and 22-24 are believed to be allowable for at least the reasons set forth above regarding claim 1. The Buck reference fails to provide the teachings noted above as missing from the Gunasingham reference. Since claims 6-8 and 22-24 are patentable at least by virtue of their dependency on claim 1, Applicants respectfully request that the rejection of claims 6-8 and 22-24 under 35 U.S.C. § 103(a) be withdrawn.

Claims 9 and 25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gunasingham et al. and Buck et al. in view of Bindra et al. Applicants respectfully traverse this rejection for the reasons discussed below.

Claims 9 and 25 are believed to be allowable for at least the reasons set forth above regarding claim 1. The Bindra reference fails to provide the teachings noted above as missing from the Gunasingham and Buck references. Since claims 9 and 25 are patentable at least by virtue of their dependency on claim 1, Applicants respectfully request that the rejection of claims 9 and 25 under 35 U.S.C. § 103(a) be withdrawn.

#### **Entry of After Final Amendment**

Applicants submit that this Amendment After Final Rejection places this application in condition for allowance by amending claims in manners that are believed to render all pending claims allowable over the cited art and/or at least place this application in better form for appeal. This Amendment is necessary to clarify pending issues and was not earlier presented because Applicants believed that the prior responses placed this application in condition for allowance, for at least the reasons discussed in those responses. Accordingly, entry of the present Amendment, as an earnest attempt to advance prosecution and/or to reduce the number of issues, is requested under 37 C.F.R. §1.116.

#### **CONCLUSION**

In view of the above remarks and amendments, Applicants respectfully submit that each of the pending objections and rejections has been addressed and overcome, placing the present application in condition for allowance. A notice to that effect is

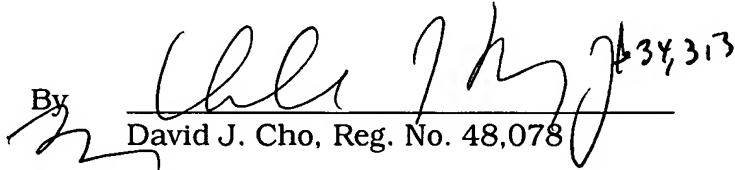
respectfully requested. Further, the above remarks demonstrate the failings of the outstanding rejections, and are sufficient to overcome the rejections. However, these remarks are not intended to, nor need they, comprehensively address each and every reason for the patentability of the claimed subject matter over the applied prior art. Accordingly, Applicants do not contend that the claims are patentable solely on the basis of the particular claim elements discussed above.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned, at the telephone number below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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